

Hepatitis C and Kidney

By

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Agenda

- Hepatitis C-related glomerular diseases
- Hepatitis C and Dialysis
- Hepatitis C and Renal Transplantation

HCV-related glomerular diseases

Is it common ?

Ann Intern Med. 2006 May 16;144(10):735-41.

Brief communication: Glomerulonephritis in patients with hepatitis C cirrhosis undergoing liver transplantation.

This study involved 30 Patients who received Liver transplantation for HCV induced cirrhosis.

A protocol renal biopsy was done in these patients.

25 out of 30 had glomerulonephritis: MPGN type 1 (n = 12), IgA nephropathy (n = 7), and mesangial glomerulonephritis (n = 6). No patient had cryoglobulins in the blood.

Immune-complex glomerulonephritis is common in patients with end-stage HCV-induced cirrhosis and is often clinically silent.

- patients with HCV have 40% higher likelihood of renal insufficiency compared to seronegative subjects.
- Subclinical and under-diagnosed glomerulopathy is frequently present in the course of the HCV infection.

- Various histological types of renal diseases are reported with HCV infection including:
 1. MPGN
 2. Membranous nephropathy
 3. FSGS
 4. Proliferative glomerulonephritis
 5. Fibrillary glomerulonephritis
 6. Immunotactoid glomerulopathy
 7. IgA nephropathy
 8. Renal thrombotic microangiopathy
 9. vasculitic renal involvement
 10. Interstitial nephritis
- Type I MPGN associated with type II mixed cryoglobulinemia (MC) is the most common HCV-associated glomerulopathy.

World J Gastroenterol 2014 June 28; 20(24): 7544-7554

- Clinical presentation:
 1. HCV-related glomerulopathy is usually asymptomatic
 2. The typical renal manifestations in HCV-infected patients include proteinuria, microscopic hematuria, hypertension, acute nephritis and nephrotic syndrome.
 3. Manifestations of MC may be present including purpura, asthenia, and arthralgia

Is screening of HCV-infected
patient necessary ?

Diagnosis:

- HCV-positive patients should be **screened** at least annually for proteinuria, microscopic hematuria, and eGFR to detect possible HCV-associated kidney disease
- Patients with proteinuria and cryoglobulinemia should be tested for HCV RNA even in the absence of clinical and/or biochemical evidence of liver disease.

kidney biopsy is indicated for patients with proteinuria, impaired renal function and cryoglobulinemia

- type I MPGN pattern of injury is the most common pathological finding.
- Vasculitis of the small- and medium-sized renal arteries
- Immunofluorescence usually demonstrates deposition of IgM, IgG, and C3 in the mesangium and capillary walls.
- On electron microscopy, subendothelial immune complexes are usually seen
- viral like particles were found within the immune complexes.

Management

- Management is either by targeting the causative pathogen or by the the pathophysiological changes resulting from it:
 1. Antiviral drugs
 2. Corticosteroids, cyclophosphamide, plasmapheresis and rituximab.

- The best long-term prognostic indicator of HCV-associated GN is **SVR** (defined as HCV RNA clearance from serum) for at least 6 months after cessation of therapy.
- There is very low–quality evidence that patients with nephrotic-range proteinuria and/or rapidly progressive kidney failure or an acute flare of cryoglobulinemia, should receive additional therapy with either plasmapheresis , rituximab or cyclophosphamide plus i.v. methylprednisolone

EASL Recommendations on Treatment of Hepatitis C 2015



- Appropriate antiviral therapy should be considered for the treatment of mixed cryoglobulinemia and renal disease associated with chronic HCV infection.
- The role of rituximab in HCV-related renal disease requires evaluation.
- The more rapid inhibition of HCV replication and high SVR rates (with DAA) will need correlation with the response of the renal injury and the cryoglobulinemia.

Are DAA safe with patients with
impaired renal function?

HCV and Dialysis

Prevalence

There is a wide range in the prevalence of HCV infection among HD patients in different parts of the world

- Varying from 1% to 90%.
- In northern Europe the prevalence rate is less than 5%
- In southern Europe and the United States around 10%
- In many countries of northern Africa, Asia and South America ranges between 10%-70%

KDIGO clinical practice guidelines for the prevention, diagnosis, evaluation, and treatment of hepatitis C in chronic kidney disease.

Kidney Int Suppl. 2008

Testing

- According to the KDIGO guidelines, either initial testing with 3rd generation ELISA or with nucleic acid testing (RT-PCR) is suggested
- If initial testing with ELISA was +ve, it should be confirmed by RT-PCR
- Yet, an **unknown** number of hemodialysis patients will test -ve for anti-HCV Ab while having detectable HCV viraemia

Hepatitis C in hemodialysis patients World J Hepatol. 2015 Mar 27

Dose these recommendations fit us ?

Are false –ve and occult HCV common
in HD patients ?

Prevalence of occult hepatitis C infection in chronic hemodialysis and kidney transplant patients

J hepatol, 2014 May

- 417 CHD & 417 Kt German patients were enrolled
- Prevalence of anti-HCV in CHD was 3.6%(15)
- Prevalence of +ve HCV RNA was 2.4%(10)
- Prevalence of HCV RNA +ve in the Anti-HCV –ve was 0% (no false negative)
- Prevalence of HCV RNA +ve in PBMC was 0.25%(1) (Occult C) of the HCV –ve patients

Occult hepatitis C virus infection in Iranian hemodialysis patients.

J Nephropathol. Oct.

- 70 Anti-HCV -ve patients on CHD enrolled
- Prevalence of +ve HCV RNA was 0% (no false –ve)
- Prevalence of +ve RNA in PBMC was 0% (no occult C)

Hepatitis C Virus (HCV) Infection among Seronegative Patients undergoing Haemodialysis in a Remotely Located Tertiary Care Hospital of Northern India: Value of HCV-RNA and Genotypes J Clin Diagn Res. 2015 Dec; 9

- 100 HD patients, anti-HCV was +ve in 30% and –ve in 70%
- HCV RNA was detected in 2.8%(2) of seronegative patients (false –ve)

Occult hepatitis C virus infection among Egyptian hemodialysis patients.

J Med Virol. 2016 Jan. 7

- 81 Anti-HCV –ve CHD patients enrolled
- Prevalence of HCV RNA +ve in PBMC while being –ve for RNA in blood was 3.7%(3) (occult C)

Occult Hepatitis C Virus Infection in Hemodialysis Patients; Single Center Study [Electron Physician 2015 Dec 20](#)

- 53 HD patients with repeatedly –ve Anti-HCV and –ve RNA in blood
- HCV RNA was detected in PBMC in 15.1%(8) of patients ([occult C](#))

High false-negative rate of anti-HCV among Egyptian patients on regular hemodialysis.

Hemodial. Inter. 2012 Jul

- 78 Anti-HCV -ve CHD patients enrolled
- Prevalence of RNA +ve results in blood was 17.9%(14) (false –ve)

Dose HCV infection on HD patients
make any difference ?

- HCV infection is associated with an increased risk for all-cause and liver-related mortality.
- Cardiovascular disease remains, however, the main cause of death in HD patients irrespective of HCV status

EASL Recommendations on Treatment of Hepatitis C Mar 2015

Hepatitis C virus and death risk in hemodialysis patients. *J Am Soc Nephrol, may 2007*

- This study was based on data analysis of a national data base of 13,664 MHD patients over 3-yr
- HCV was associated with higher all-cause and **cardiovascular mortality** across almost all clinical, demographic, and laboratory groups of patients.

Which patients to treat ?

- Antiviral therapy should be considered for HD patients particularly those who will be candidates for renal transplantation.

EASL Recommendations on Treatment of Hepatitis C Mar 2015

- AASLD recommended initiation of therapy for **all** patients with chronic HCV infection except those with short life expectancy.

*Recommendations for Testing, Managing, and Treating Hepatitis C
,2016 Feb 24*

HCV and Renal Transplantation

Risk of HCV in Renal Transplant Recipients

- Progression of liver fibrosis is increased after transplantation with increased incidence of complications including HCC

Yet, this is not a solid fact. Some studies showed that the course of liver disease was not changed. This depends on:

1. Degree of liver fibrosis at time of transplant.
2. Type of immunosuppressives used (cyclosporin suppresses liver fibrosis)

- HCV is a risk factor for impaired graft survival whether related or not related to the development of HCV related glomerulopathy in the graft

- Long term survival is decreased in HCV-infected recipients compared to HCV-uninfected recipients
- All cause and liver related mortality are increased

Yet, survival is still much better than HCV-infected patients who remain on HD

- Hepatitis C in non-hepatic solid organ transplant candidates and recipients: A new horizon Worl J Gastroentrol. 2016 Jan 28
- EASL Recommendations on Treatment of Hepatitis C Mar 2015

Treat HCV before or after
Transplantation ?

- HCV treatment before kidney transplantation may avoid liver-related mortality in the post-transplant patient, and may prevent HCV-specific causes of renal graft dysfunction.
- Where possible, antiviral therapy should be given to potential transplant recipients before listing for renal transplantation.

EASL Recommendations on Treatment of Hepatitis C Mar 2015

What about HCV-positive Donors ?

THANK YOU